

IN THE SPECIFICATION:

On page 2, please amend the paragraph beginning at line 25 as follows:

In one embodiment, the invention features an isolated nucleic acid molecule that includes the nucleotide sequence set forth in SEQ ID NO:1 or SEQ ID NO:3. In another embodiment, the invention features an isolated nucleic acid molecule that encodes a polypeptide including the amino acid sequence set forth in SEQ ID NO:2. ~~In another embodiment, the invention features an isolated nucleic acid molecule that includes the nucleotide sequence contained in the plasmid deposited with ATCC® as Accession Number _____.~~

On pages 10 and 11, please amend the paragraph beginning at line 37 of page 10 as follows:

In a preferred embodiment, an HGT-1 polypeptide includes at least one or more of the following domains: a transmembrane domain and/or a galactosyltransferase family domain, and has an amino acid sequence at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or more homologous or identical to the amino acid sequence of SEQ ID NO:2, ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____.~~ In yet another preferred embodiment, an HGT-1 polypeptide includes at least one or more of the following domains: a transmembrane domain and/or a galactosyltransferase family domain, and is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a complement of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3. In another preferred embodiment, an HGT-1 polypeptide includes at least one or more of the following domains: a transmembrane domain and/or a galactosyltransferase family domain, and has an HGT-1 activity.

On page 12, please amend the paragraph beginning at line 3 as follows:

The nucleotide sequence of the isolated human HGT-1 cDNA and the predicted amino acid sequence of the human HGT-1 polypeptide are shown in Figures 1A-1C and in SEQ ID NOs:1 and 2, respectively. ~~A plasmid containing the nucleotide sequence encoding human HGT-1 was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on _____ and assigned Accession Number _____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

On page 13, please amend the paragraph beginning at line 5 as follows:

A nucleic acid molecule of the present invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, as a hybridization probe, HGT-1 nucleic acid molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, J. *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

On page 13, please amend the paragraph beginning at line 16 as follows:

Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1 or 3, ~~or the~~

~~nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____.~~

On page 14, please amend the paragraph beginning at line 6 as follows:

In still another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, thereby forming a stable duplex.

On page 14, please amend the paragraph beginning at line 18 as follows:

In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or more identical to the nucleotide sequence shown in SEQ ID NO:1 or 3 (*e.g.*, to the entire length of the nucleotide sequence), ~~or to the nucleotide sequence (*e.g.*, the entire length of the nucleotide sequence) of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion of any of these nucleotide sequences. In one embodiment, a nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least (or no greater than) 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 615, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000, 2050, 2100, 2150, 2200, 2250, 2300, 2350, 2400, 2450, 2500, 2550, 2600,

2650, 2700, 2750, 2800, 2850, 2900, 2950, 3000, 3050, 3100, 3150, 3200, 3250, 3300, 3350, 3400, 3450, 3500, 3550, 3600, 3650, 3700, 3750, 3800, 3850, 3900, 3950, 4000 or more nucleotides in length and hybridizes under stringent hybridization conditions to a complement of a nucleic acid molecule of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____.~~

On pages 14 and 15, please amend the paragraph beginning at line 36 of page 14 as follows:

Moreover, the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____,~~ for example, a fragment which can be used as a probe or primer or a fragment encoding a portion of an HGT-1 polypeptide, *e.g.*, a biologically active portion of an HGT-1 polypeptide. The nucleotide sequence determined from the cloning of the HGT-1 gene allows for the generation of probes and primers designed for use in identifying and/or cloning other HGT-1 family members, as well as HGT-1 homologues from other species. The probe/primer typically comprises substantially purified oligonucleotide. The probe/primer (*e.g.*, oligonucleotide) typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, 75, 80, 85, 90, 95, or 100 or more consecutive nucleotides of a sense sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____,~~ of an anti-sense sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____,~~ or of a naturally occurring allelic variant or mutant of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____.~~

On pages 15 and 16, please amend the paragraph beginning at line 31 of page 15 as follows:

A nucleic acid fragment encoding a "biologically active portion of an HGT-1 polypeptide" can be prepared by isolating a portion of the nucleotide sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as~~

~~Accession Number _____~~, which encodes a polypeptide having an HGT-1 biological activity (the biological activities of the HGT-1 polypeptides are described herein), expressing the encoded portion of the HGT-1 polypeptide (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the HGT-1 polypeptide. In an exemplary embodiment, the nucleic acid molecule is at least 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 615, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000, 2050, 2100, 2150, 2200, 2250, 2300, 2350, 2400, 2450, 2500, 2550, 2600, 2650, 2700, 2750, 2800, 2850, 2900, 2950, 3000, 3050, 3100, 3150, 3200, 3250, 3300, 3350, 3400, 3450, 3500, 3550, 3600, 3650, 3700, 3750, 3800, 3850, 3900, 3950, 4000 or more nucleotides in length and encodes a polypeptide having an HGT-1 activity (as described herein).

On page 16, please amend the paragraph beginning at line 8 as follows:

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. Such differences can be due to degeneracy of the genetic code, thus resulting in a nucleic acid which encodes the same HGT-1 polypeptides as those encoded by the nucleotide sequence shown in SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a polypeptide having an amino acid sequence which differs by at least 1, but no greater than 5, 10, 20, 50 or 100 amino acid residues from the amino acid sequence shown in SEQ ID NO:2, ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number _____~~. In yet another embodiment, the nucleic acid molecule encodes the amino acid sequence of human HGT-1. If an alignment is needed for this comparison, the sequences should be aligned for maximum homology.

On pages 16 and 17, please amend the paragraph beginning at line 36 of page 16 as follows:

Accordingly, in one embodiment, the invention features isolated nucleic acid molecules which encode a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, ~~or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, wherein the nucleic acid molecule hybridizes to a complement of a nucleic acid molecule comprising SEQ ID NO:1 or SEQ ID NO:3, for example, under stringent hybridization conditions.

On page 17, please amend the paragraph beginning at line 25 as follows:

Moreover, nucleic acid molecules encoding other HGT-1 family members and, thus, which have a nucleotide sequence which differs from the HGT-1 sequences of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ are intended to be within the scope of the invention. For example, another HGT-1 cDNA can be identified based on the nucleotide sequence of human HGT-1. Moreover, nucleic acid molecules encoding HGT-1 polypeptides from different species, and which, thus, have a nucleotide sequence which differs from the HGT-1 sequences of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ are intended to be within the scope of the invention. For example, a mouse HGT-1 cDNA can be identified based on the nucleotide sequence of a human HGT-1.

On page 18, please amend the paragraph beginning at line 5 as follows:

Orthologues, homologues and allelic variants can be identified using methods known in the art (*e.g.*, by hybridization to an isolated nucleic acid molecule of the present invention, for example, under stringent hybridization conditions). In one embodiment, an isolated nucleic acid molecule of the invention is at least 15, 20, 25, 30 or more nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In other embodiment, the nucleic acid is at least 50, 75,

100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000, 2050, 2100, 2150, 2200, 2250, 2300, 2350, 2400, 2450, 2500, 2550, 2600, 2650, 2700, 2750, 2800, 2850, 2900, 2950, 3000, 3050, 3100, 3150, 3200, 3250, 3300, 3350, 3400, 3450, 3500, 3550, 3600, 3650, 3700, 3750, 3800, 3850, 3900, 3950, 4000 or more nucleotides in length.

On pages 19 and 20, please amend the paragraph beginning at line 25 of page 19 as follows:

In addition to naturally-occurring allelic variants of the HGT-1 sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, thereby leading to changes in the amino acid sequence of the encoded HGT-1 polypeptides, without altering the functional ability of the HGT-1 polypeptides. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of HGT-1 (*e.g.*, the sequence of SEQ ID NO:2) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the HGT-1 polypeptides of the present invention, *e.g.*, those present in a transmembrane domain and/or a galactosyltransferase family domain, are predicted to be particularly unamenable to alteration. Furthermore, additional amino acid residues that are conserved between the HGT-1 polypeptides of the present invention and other members of the HGT-1 family are not likely to be amenable to alteration.

On pages 20 and 21, please amend the paragraph beginning at line 14 of page 20 as follows:

An isolated nucleic acid molecule encoding an HGT-1 polypeptide identical to the polypeptide of SEQ ID NO:2, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded polypeptide. Mutations can be introduced into SEQ ID NO:1 or 3; ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in an HGT-1 polypeptide is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an HGT-1 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for HGT-1 biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, the encoded polypeptide can be expressed recombinantly and the activity of the polypeptide can be determined.

On page 23, please amend the paragraph beginning at line 10 as follows:

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haseloff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave HGT-1 mRNA transcripts to thereby inhibit translation of HGT-1 mRNA. A ribozyme having specificity for an HGT-1-encoding nucleic acid can be designed based upon the nucleotide sequence of an HGT-1 cDNA disclosed herein (*i.e.*, SEQ ID NO:1 or 3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an HGT-1-encoding mRNA. See, *e.g.*, Cech *et al.*, U.S. Patent No. 4,987,071; and Cech *et al.*, U.S. Patent No. 5,116,742. Alternatively, HGT-1 mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

On pages 26 and 27, please amend the paragraph beginning at line 31 of page 26 as follows:

Another aspect of the invention features fragments of the polypeptide having the amino acid sequence of SEQ ID NO:2, for example, for use as immunogens. In one embodiment, a fragment comprises at least 5 amino acids (*e.g.*, contiguous or consecutive amino acids) of the amino acid sequence of SEQ ID NO:2, ~~or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number _____~~. In another embodiment, a fragment comprises at least 10, 15, 20, 25, 30, 35, 40, 45, 50 or more amino acids (*e.g.*, contiguous or consecutive amino acids) of the amino acid sequence of SEQ ID NO:2, ~~or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number _____~~.

On pages 40 and 41, please amend the paragraph beginning at line 32 of page 40 as follows:

A transgenic animal of the invention can be created by introducing an HGT-1-encoding nucleic acid into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The HGT-1 cDNA sequence of SEQ ID NO:1 can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of a human HGT-1 gene, such as a mouse or rat HGT-1 gene, can be used as a transgene. Alternatively, an HGT-1 gene homologue, such as another HGT-1 family member, can be isolated based on hybridization to the HGT-1 cDNA sequences of SEQ ID NO:1 or 3, ~~or the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ (described further in subsection I above) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to an HGT-1 transgene to direct expression of an HGT-1 polypeptide to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, both by Leder *et al.*, U.S. Patent No. 4,873,191 by Wagner *et al.* and in Hogan, B., *Manipulating the Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of an HGT-1 transgene in its genome and/or expression of HGT-1 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding an HGT-1 polypeptide can further be bred to other transgenic animals carrying other transgenes.

On page 62, please amend the paragraph beginning at line 6 as follows:

An exemplary method for detecting the presence or absence of HGT-1 polypeptide or nucleic acid in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting HGT-1

polypeptide or nucleic acid (*e.g.*, mRNA, or genomic DNA) that encodes HGT-1 polypeptide such that the presence of HGT-1 polypeptide or nucleic acid is detected in the biological sample. In another aspect, the present invention provides a method for detecting the presence of HGT-1 activity in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of HGT-1 activity such that the presence of HGT-1 activity is detected in the biological sample. A preferred agent for detecting HGT-1 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to HGT-1 mRNA or genomic DNA. The nucleic acid probe can be, for example, the HGT-1 nucleic acid set forth in SEQ ID NO:1 or 3, ~~or the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to HGT-1 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

On page 80, please amend the paragraph beginning at line 10 as follows:

The invention is based, at least in part, on the discovery of a human gene encoding a novel polypeptide, referred to herein as human HGT-1. The entire sequence of the human clone 8797 was determined and found to contain an open reading frame termed human "HGT-1." The nucleotide sequence of the human HGT-1 gene is set forth in Figures 1A-1C and in the Sequence Listing as SEQ ID NO:1. The amino acid sequence of the human HGT-1 expression product is set forth in Figures 1 and in the Sequence Listing as SEQ ID NO:2. The HGT-1 polypeptide comprises 378 amino acids. The coding region (open reading frame) of SEQ ID NO:1 is set forth as SEQ ID NO:3. ~~Clone 8797, comprising the coding region of human HGT-1, was deposited with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on _____, and assigned Accession No. _____.~~